comprises a fragment of at least about 10 nucleotides.

31. The composition of matter of claim 12, wherein said polynucleotide comprises a fragment of at least about 12 nucleotides.

32. The composition of matter of claim 12, wherein said polynucleotide comprises a fragment of at least about 15 ~~nucleotides~~.

33. The composition of matter of claim 12, wherein said polynucleotide comprises a fragment of at least about 20 nucleotides.--

REMARKS

Introductory Comments

Claims 1-15 are pending. Claims 7-10 and 13 have been withdrawn from consideration. Claim 14 is not addressed in this response (see below). New claims 16-33 have been entered by this amendment.

The Examiner has rejected claims 12, 14 and 15 under 35 U.S.C. §101, asserting that the claims are directed to non-statutory matter.

The Examiner has rejected claims 1-6, 11, 12, 14 and 15 under 35 U.S.C. §112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Examiner has rejected claim 1-4 and 12 under 35 U.S.C. §102(b) asserting that the claim is anticipated by Hillier, et al., (GenBank Accession T94049).

The Examiner has rejected claims 1-3 under 35 U.S.C. §102(b) asserting that the claim is anticipated by the NEB 1994/1995 catalog.

The Examiner has rejected claims 5, 6 and 11 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Hillier, et al., (GenBank Accession T94049) in view

of Ausubel.

These rejections are believed to be overcome in part by the amendments and are otherwise traversed for reasons discussed below.

Overview of the Amendments

Claim 15 has been canceled without prejudice or disclaimer. Claims 1, 4, 5, 11, and 12 have been amended without prejudice or disclaimer. Cancellation or amendment of these claims is not intended to be an acquiescence in the Office's assessment of those claims in the 12 May 1999 Communication, and applicants expressly reserve the right to bring the subject matter of the original claims again in a subsequent, related application.

Basis for the amendment to claim 1 can be found throughout the specification, for example, at the following locations: in originally presented claim 1; and Example 1, pages 57-59. Further basis for the amendment to claim 1, in particular dealing with the language "specifically binds," is discussed below in the section dealing with the rejections under 35 U.S.C. §112, second paragraph.

Basis for the amendment to claim 5 can be found throughout the specification, for example, at the following locations: originally presented claim 5; "an open reading frame of at least 5 amino acids," e.g., at page 17, lines 13-26, page 18, lines 6-14, page 14, lines 29-34; and, "nucleotides 51-284 of SEQUENCE ID NO 7," e.g., page 58, lines 30-34.

Basis for the amendment to claim 11 can be found throughout the specification, for example, at the following locations: originally presented claim 11; page 18, lines 23-29; and page 14, lines 8-34..

Basis for the amendment to claim 12 can be found throughout the specification, for example, at the following locations: originally presented claim 12; and page 16, lines 20-27. Basis for "specifically binds" is discussed below in the section dealing with the rejections under 35 U.S.C. §112, second paragraph.

Basis for new claims 16, 17, and 18 can be found throughout the specification, for example, at the following locations: page 17, lines 5-17; and page 18, lines 6-8.

Basis for new claim 19 can be found throughout the specification, for example, at the following locations: originally presented claim 11; and page 58, lines 30-34.

Basis for new claims 20-21 and 28-29 can be found throughout the specification, for example, at the following locations: page 18, lines 23-29.

Basis for new claims 22-25 and 30-33 can be found throughout the specification, for example, at the following location: page 14, lines 8-34 .

Basis for new claim 26 can be found throughout the specification, for example, at the following locations: originally presented claim 1; and page 58, lines 30-34.

Basis for new claim 27 can be found throughout the specification, for example, at the following locations: originally presented claims 1 and 11; and page 58, lines 30-34.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

Addressing the Examiner's Objections and Rejections

1. Election/Restriction

The Examiner states the following: "Claims 1-15 are pending. Claims 7-10, 13, and 14 have been withdrawn from consideration as being drawn to non-elected inventions. Claims 1-6, 11-12, and 15 are examined on the merits." (Office action, dated 12 May 1999, page 2, point 2.) However, on page 3 in the rejections under 35 U.S.C. §101 and §112 the Examiner has rejected claim 14 and on the first page of the Office action it was indicated that claim 14 was rejected. The applicants have assumed, for the sake of the current response, that claim 14 is not pending. Applicants have made this assumption based on (i) the Examiner's statement on page 2 of the Office action, (ii) the initial restriction requirement, and (iii) the fact that claim 14 is directed to a polypeptide coding sequence and the rest of the pending claims are directed to polynucleotide sequences.

In view of the foregoing, applicants request clarification of which claims have been examined on the merits.

2. Objection to the Claim to Priority

The Examiner has acknowledged applicants' claim for priority under 35 U.S.C. 119(e) to U.S. Provisional Application Serial No. 60/048,810 ('810); however, the Examiner asserts that a priority claim to SEQ ID NOS:1-7 of the present application is not supported because different sequences are disclosed as SEQ ID NOS:1-7 in the provisional application '810. Applicants believe this assertion is in error. A comparison of SEQ ID NO:7 (the consensus sequence) of the present application with SEQ ID NO:9 (the consensus sequence) of the provisional application '810 results in 100% sequence identity from nucleotide positions 5-419 in SEQ ID NO:7 compared to nucleotide positions 1-415 in SEQ ID NO:9 ('810). Further, the 78 amino acid open reading frame (ORF) identified in '810 and presented as SEQ ID NO:12 ('810) has 100% identity to the 78 amino acid open reading frame (ORF) identified in the present application (page 58, lines 30-33) as SEQ ID NO:15.

Accordingly, the applicants submit that the Examiner's conclusion was erroneous and that, in fact, the applicants are entitled to their priority date of 5 June 1997 for the presently claimed sequences.

3. Objections to the Drawings

The applicants request that the requirement for submission of formal drawings be held in abeyance until the indication of allowable subject matter by the Examiner.

4. Rejection of Claims 12, 14 and 15 under 35 U.S.C. §101

The Examiner has rejected claims 12, 14 and 15 under 35 U.S.C. §101, asserting that the claims are directed to non-statutory matter. The applicants will not respond to the rejection of claim 14 for the reasons discussed above. Claim 15 has been canceled by this amendment, without prejudice or disclaimer.

Claim 12 has been amended per the Examiner's suggestion to include the language a "composition of matter comprising a purified polynucleotide." Applicants

thank the Examiner for his suggestion. Accordingly, the applicants submit that the invention is now directed to statutory subject matter. Withdrawal of the rejection of the claims under 35 U.S.C. §101 is, therefore, respectfully requested.

5. Rejection of Claims 1-6, 11, 12, 14 and 15 under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-6, 11, 12, 14 and 15 under 35 U.S.C. §112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. In particular, the Examiner asserts that recitation of "% identity" in claims 1, 5, 12 and 15 is vague and indefinite.

The applicants respectfully disagree with the Examiner's position. On page 12, line 35, to page 13, line 18, the applicants discuss the use of available programs for calculating identity or similarity between sequences, in particular the applicants state the following:

> "Two or more polynucleotide sequences can be compared by determining their "percent identity." Two or more amino acid sequences likewise can be compared by determining their "percent identity." The programs available in the Wisconsin Sequence Analysis Package, Version 8 (available from Genetics Computer Group, Madison, WI), for example, the GAP program, are capable of calculating both the identity between two polynucleotides and the identity and similarity between two polypeptide sequences, respectively." (Specification, page 13, lines 11-17.)

The applicants submit that use of default parameters in the GAP program (as described in the User Manual) is routine and well within the abilities of one having ordinary skill in the art.

Absolute specificity and precision are not required in the claims. Claims need only reasonably apprize a person having ordinary skill in the art as to their scope. *Hybritech Inc., v. Monoclonal Antibodies, Inc.,* 231 USPQ 81, Fed. Cir. 1986. The

second paragraph of 35 U.S.C. §112 merely requires that an applicant set out and circumscribe a particular subject area with a reasonable degree of precision such that the metes and bounds of the invention are set forth. *Ex parte Head*, 214 USPQ 551, PTO Bd. App. 1981.

However, in an effort to facilitate prosecution, applicants have deleted the language "percent identity" from the pending claims, as suggested by the Examiner. Applicants have introduced the language " a polynucleotide that specifically binds to a polynucleotide sequence." The specification provides extensive basis for use of this language. For example, on page 20, line 27, to page 21, line 7, detection of an analyte is discussed wherein a specific binding member is prepared for binding to a target analyte such as a nucleotide target. On page 21, lines 24-36, a definition of "specific binding members" is discussed, wherein a "specific binding member" is a member of a specific binding pair (see also, e.g., page 22, lines 11-26; page 24; and page 6, line 4, to page 7, line 32). That is, two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Specific binding pairs can include complementary nucleotide sequences. On pages 27-28, the specification describes how the sequences provided in the application may be used to produce polynucleotide sequences (for example, primers and probes; also see, e.g., page 14, line 35, to page 15, line 6) which can be used in assays for the detection of target nucleic acids in test samples, via specifically binding the polynucleotide sequences to the target. Probes may, for example, be designed from conserved nucleotide regions of the polynucleotides of interest or from non-conserved nucleotide regions of the polynucleotide of interest. The design of such probes for optimization in assays is within the skill of the routineer. Generally, nucleic acid probes are developed from non-conserved or unique regions when maximum specificity is desired, and nucleic acid probes are developed from conserved regions when assaying for nucleotide regions that are closely related to, for example, different members of a multi-gene family or in related species like mouse and man. Numerous examples are given in the specification that

would allow one of ordinary skill in the art to determine the metes and bounds of the invention (e.g., Examples 1-9, pages 57-70). For example, selection of primers for use in polymerase chain reactions is described at least on page 27, line 33, to page 29, line 5, and exemplary conditions (including hybridization conditions) for such reactions are described in the Examples (e.g., Examples 3, 8 and 9).

Use of probes in fluorescent in situ hybridization (FISH) technology to perform chromosomal analysis is also described herein. Such an approach can be used to identify cancer-specific structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR-generated and/or allele specific oligonucleotides probes, allele specific amplification or by direct sequencing. Probes also can be labeled with radioisotopes, directly- or indirectly- detectable haptens, or fluorescent molecules, and utilized for *in situ* hybridization studies to evaluate the mRNA expression of the gene comprising the polynucleotide in tissue specimens or cells (page 27, lines 9-20; and Example 7, pages 66-67). Use of the polynucleotide sequences of the present invention in such technology is another example of specific binding of a polynucleotide sequence to a target.

The characteristics and properties of polynucleotides of the present invention for use in hybridization reactions (including probes and amplification primers) are extensively discussed in the specification in the context of specific binding (see, for example, pages 27-34). Further, examples using polynucleotides in hybridization reactions are discussed in the application, including suitable reaction conditions (e.g., Examples 5, 6, and 7, pages 64-67).

The court has consistently stated that claim language must be read in light of prior art and teachings of the specification. The standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971). A claim which is clear to one ordinarily skilled in the art when read in light of the

specification, does not fail for indefiniteness. *Slimfold Mfg. Co. v. Kinkead Indus., Inc.*, 932 F2d 1453, 1 USPQ2d 1536 (Fed. Cir 1986).

In view of the above amendments, the teachings of the specification and the level of ordinary skill in the present art, the applicants submit that the boundaries of the claims are capable of being understood by one of ordinary skill in the art. Therefore, withdrawal of the rejection of the claims under 35 U.S.C. §112, second paragraph, is respectfully requested.

6. Rejection of Claims 1-4, and 12 Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1-4 and 12 under 35 U.S.C. §102(b) asserting that the claim is anticipated by Hillier, et al., (GenBank Accession T94049).

Further, the Examiner has rejected claims 1-3 under 35 U.S.C. §102(b) asserting that the claim is anticipated by the NEB 1994/1995 catalog.

For prior art to anticipate under 35 U.S.C. 102 it has to meet every element of the claimed invention: such a determination is one of fact. *Hybritech Inc. v. Monoclonal Antibodies*, 802 F.2d at 1367, 231 USPQ 81 (Fed. Cir. 1986).

The prior art sequences do not teach all the elements of the pending independent claims, as described in the following discussion. The accompanying figure (Appendix A) shows a rough alignment of the cited sequence relative to the claimed sequences of the present invention. The alignments were based on the "query" sequence beginning and end locations as recited in the MPSRCH alignments. The following can be seen from the comparisons in the figures:

(i) none of the sequences anticipate any of the complete claimed sequences (i.e., intact SEQUENCE ID NO 1, SEQUENCE ID NO 2, SEQUENCE ID NO 3, and nucleotides 51-284 of SEQUENCE ID NO 7);

(ii) fragments of any of SEQUENCE ID NOs 1, 2, and 3 cannot be anticipated by the sequences cited by the Examiner; and

(iii) a nucleic acid sequence that encodes an open reading frame of at least 5

amino acids derived from a polynucleotide selected from the group consisting of SEQUENCE ID NO 1, SEQUENCE ID NO 2, SEQUENCE ID NO 3, and nucleotides 51-284 of SEQUENCE ID NO 7 are not anticipated by the sequences cited by the Examiner.

In view of the above amendments and arguments, the cited reference sequences cannot be said to teach all the elements of the present invention. The dependent claims distinguish over the prior art at least in view of their dependencies on the independent claims. Accordingly, there is no support for the pending claims being anticipated by the cited prior art under 35 U.S.C. §102(b) and withdrawal of the rejection is respectfully requested.

7. Rejections of the Claims Under 35 U.S.C. §103

The Examiner has rejected claims 5, 6 and 11 under 35 U.S.C. §103(a) as being unpatentable over Hillier, et al., (GenBank Accession T94049) in view of Ausubel.

As discussed above, the reference of Hillier, et al., does not teach all the limitations of the independent claims. Ausubel (a general methodology reference) does not make up for the shortcomings of the Hillier, et al., reference.

Accordingly, in view of the above information and arguments, applicants respectfully request that the rejection of the claims under 35 U.S.C. §103 be withdrawn.

CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Please direct all further communications in this application to:

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Respectfully submitted,

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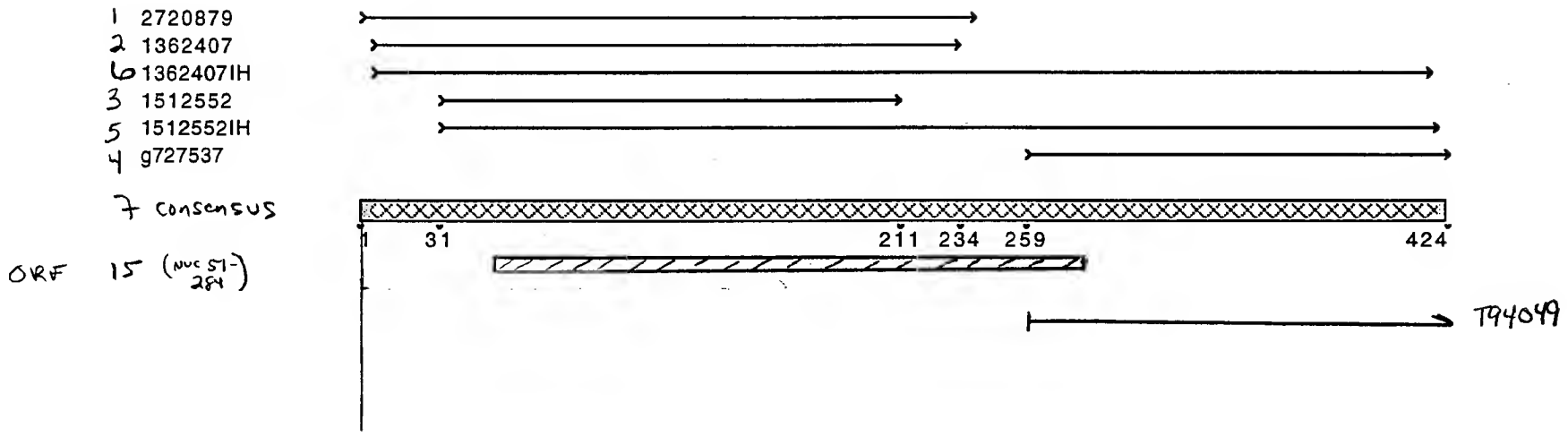
Appendix A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2 1362407
6 1362407IH
3 1512552
5 1512552IH
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7 consensus
1
31
211
234
259
424
ORF 15 (nuc 57-284)
T94049